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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/230,195	12/10/99	RYBAK	S 015280-28410

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EXAMINER	
SORBELLO, E	
ART UNIT	**PAPER NUMBER**
1633	10

DATE MAILED: 11/08/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/230,195	Applicant(s) RYBAK ET AL.	
	Examiner Eleanor Sorbello	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35,37,38 and 40-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35 and 41* is/are rejected.

7)☒ Claim(s) *37,38 and 40* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

R sponse to amendment

1. Applicant's amendment and response to the official Office Action mailed February 16, 2001 as Paper No. 6, has been received and filed on August 7, 2001 as Paper No. 7A. Claims 11, 37, 38, 40 have been amended, claims 36, 39 have been canceled. **Claims 1-35, 37, 38, 40-42 are pending.**

Receipt of IDS dated 08/17/01 is acknowledged.

Applicant's amendments and arguments have been thoroughly reviewed, and are partially persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's argument.

2. Applicant's arguments are addressed below on a per section basis.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-35, 41, 42 remain rejected as stated in Office Action dated February 16, 2001 under 35 USC § 112, first paragraph for reasons of record. Applicant's arguments have been fully considered but they are not persuasive.

Claims 1-35, 41 and 42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) a cell transduction plasmid vector based on a HIV-lentiviral vector comprising a nucleic acid sequence encoding a

retroviral packaging site, a splice donor (SD) , splice acceptor (SA); a retroviral Rev binding sequence, a IRES promoter sequence operably linked to the first viral inhibitor sequence wherein the inhibitor sequence is located between the SD and SA sequence, wherein the inhibitor sequence integrates into the nucleus of the cell; does not reasonably provide enablement for any transduction vector comprising the aforementioned limitations including subsequences for the viral inhibition comprising SD site subsequences, SA site subsequence and Rev subsequences, including the limitations encompassed by the claims . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicants argue that examiner rejected the claims based on the fact that applicants did not provide specifically what part of the sequence constituted the subsequence. (See Response page 4, paragraph 1). However, the part of the sequence that is functional and that which will function operably with the other sequences such as the viral vector subsequence, DS, SA, Rev is not predictable in view of the breadth of the claim and the unpredictability of combining several sub-sequences in tandem without support in the specification as to what parts of the entire sequence would or would not work. As such the rejection with regard to the aforementioned issue stands.

Applicants argue that the claims drawn to a viral inhibitor that is an antibody binding to a ras protein or an RNase is taught in the specification. (See Response page 4, paragraph 2). However, the claims are directed to a transduction vector, wherein

vector targets a specific cell, enters it and in the case of the retroviral vector binds to the cell genome and thereby the two viral inhibitors are in place to function in producing the viral inhibitors. However the specification does not support such except by prophetic consideration. As stated in the first office action on merits, targeting vectors are currently being developed and therefore lack extensive support in the prior art. It is therefore incumbent on the applicants to provide support for that which is not provided for in the prior art. As such the rejection stands.

Applicants argue that undue experimentation is not necessary to produce any vector for all transgenes that targets all types of cells. Applicants also argue that in order to consider if undue experimentation is necessary the examiner should consider the support in the specification in light of the Wands factors. Applicants also state that the USPTO training guidelines do not require that each and every nucleic acid is recited in the case of applications involving a large number of potential nucleic acids. (See pages 5 - page 6, paragraph 2). However the references provided in the First Office Action dated 2/16/01 by Deonarain teach that targeting vectors are currently being developed and therefore if one vector is modified for targeting one cell type for a specific function it does not mean that one of skill in the art will be able to without undue experimentation to make any and all vectors. Crystal (1995, Science, Vol. 270, page 404-410) (also provided in the first office action) also reviews various vectors known in the art and indicates that "among the design hurdles for all vectors is the need to increase the efficiency of gene transfer, to increase target specificity and to enable the transferred gene to be regulated" (page 409).

Therefore, in view of the breadth of the claims, nature of the art, lack of support in the specification, one of skill in the art, will require undue experimentation to make the invention as claimed.

5. Claims 20 and 26 stand rejected as stated in Office Action dated 2/16/01, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for transduction vectors consisting of pBAR; pBAR-ONC and pBAR-EDN, does not reasonably provide enablement for any conservative modifications of the aforementioned vectors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification teaches the construction of vectors pBAR, pBAR-ONC and pBAR-EDN but does not teach each and every conservative amino acid modification as claimed.

Applicants argue (on page 6, last paragraph of Response dated 8/7/01), that the specification teaches the modifications that could be made to the vectors stated above. Applicants state that the specification teaches modifications such as delta-gag, various RNAses including Onconase and modified onconases. The applicants also state that they have taught (See page 13, lines 25-31 of specification) conservatively modified variants. However, the specification merely states the degenerate genetic code encoding amino acids. Therefore as stated in the First Office Action, and the supporting

reference by Ding which indicates that substitutions, deletions, etc in a polypeptide is unpredictable with respect to the functionality, the claims remain rejected.

6. Claim 29 stands rejected as stated in Office Action dated February 16, 2001 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This claim still reads on a vector for transducing a cell with a nucleic acid *in vivo* and therefore remains rejected for reasons of record.

Conclusion

7. Claims 1-35, 41-42 are rejected.

8. Claims 37, 38, 40 are objected to because the claims depend from a rejected claim.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication should be directed to Eleanor Sorbello, who can be reached at (703)-308-6043. The examiner can normally be reached on Mondays-Fridays from 6.30 a.m. to 3.00 p.m. EST.

Questions of formal matters can be directed to the patent analyst, Tracey Johnson, whose telephone number is (703) 305-2982.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

If the claims are amended canceled and/or added the applicants are required to follow Amendment Practice under 37 CFR § 1.121 *(http://www.uspto.gov)* and A CLEAN COPY OF **ALL** PENDING CLAIMS IS REQUESTED to facilitate further examination.

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER